

# The cervical extension of human fetal thymus

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## Abstract

**Introduction:** Thymus is a primary central lymphoid organ, responsible for provision of the T- lymphocytes to the entire body. It is a soft bilobed organ consisting of a pair of laterally compressed, more or less pyramidal lobes, lying close together side by side, joined in the midline by the connective tissue which merges with the capsule of each lobe. The greater part of the organ lies in the superior and the anterior inferior mediastinum, the lower border reaching the level of the 4<sup>th</sup> costal cartilage. Superior extension into the neck is common, sometimes reaching the inferior pole of the thyroid gland or even higher. In the present study 53 human fetuses (24 male and 29 female) of different age groups ranging from 9<sup>th</sup> to 40<sup>th</sup> weeks of gestational age were dissected at department of anatomy, Government medical college, Aurangabad. All the specimens were located in the superior and anterior inferior mediastinum. However in one fetus of 20 weeks upper pole was extended high up into the neck but it did not reach to thyroid gland. In young children a large thymus may press on the trachea causing attacks of respiratory stridor. Cervical thymic anomalies must be considered as a differential diagnosis for children presenting with neck masses.

**Keywords:** Thymus, Cervical extension, Anatomical variation.

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## INTRODUCTION

The thymus is now accepted as a key stone of the defence mechanism of the body.<sup>1</sup> It is the first organ of the immune system in which the lymphocytes appear and continues to be the most active lymphopoietic tissue throughout the embryonic life.<sup>2</sup> It is a primary central lymphoid organ, responsible for provision of the T- lymphocytes to the entire body. It provides a unique microenvironment in which T- cell precursors (thymocytes) undergo development, differentiation and colonial expansion, during this process they are 'educated' to react with exquisite specificity against foreign antigen and achieve immune tolerance to body's

own components. Thymus is also a part of the neuroendocrine axis of the body, and it both influences and is influenced by the products of this axis.<sup>3</sup> The first stage of thymic development is seen bilaterally in the third pharyngeal pouch towards the end of 6<sup>th</sup> gestational week, when endodermal cells form a sacculation. The lower ends enlarge and unite superficially at 8<sup>th</sup> week. The lower ends are attached to the pericardium and gradually sink with it to a permanent position in thorax where it is located in the superior and anterior inferior mediastinum, the lower border reaches up to 4<sup>th</sup> costal cartilage.<sup>3,4</sup> Defective pathways of the embryological descent of the thymic primordia may lead to a clinical spectrum of anomalies of the thymus.<sup>5</sup> There have been reports of various combinations of cystic and solid thymus, such as accessory cervical thymus (sequestration and failure of involution), cervical thymic cyst, completely undescended cervical thymus, persistent thymopharyngeal duct, persistent thymic cord directly attached to the mediastinal thymus, and cervical extension of mediastinal thymus.<sup>6-10</sup> Furthermore, ectopic thymic tissue may lead to the development of some lesion, including thymic cyst, ectopic cervical thymus (as a mass), and cervical thymoma.<sup>11</sup> 80% to 90% of patients are asymptomatic and have only a painless

swelling.<sup>12,13,14,15</sup> Respiratory symptoms such as dyspnea, hoarseness, stridor, and dysphagia are reported in 6% to 13% of patients.<sup>10</sup> Progressive airway obstruction secondary to a rapidly enlarging cervical thymic cyst has been reported in neonates.<sup>13,14,16</sup>

## MATERIAL AND METHOD

Ethical approval was obtained from institutional ethics committee for the present study, 53 human fetuses (24 male and 29 female) of different age groups ranging from 9<sup>th</sup> to 40<sup>th</sup> weeks of gestational were procured from the department of Obstetrics and Gynaecology, Government medical college, Aurangabad for research work with due permission from the Professor and Head of the department and consent from respective parents. These fetuses included the spontaneous abortuses, still born and terminated fetuses under the Medical Termination of Pregnancy Act of India 1971. Only the fetuses free from detectable abnormality belonging to the mother with normal obstetrical history were taken into consideration for the study. Twins and fetuses with gross anomalies were omitted. Fetuses were obtained within 4-5 hrs of birth to avoid post-mortem changes. Gestational age of the foetuses is determined by Crown-rump length (CRL). The sternoclavicular joints were disarticulated and costal cartilages were cut (Photograph-1). Thus the entire thoracic cavity was open and lower part of neck was also dissected for complete exposure of thymus in its natural location (Photograph-2). It was removed carefully without fat and the connective tissues and placed on a moistened sponge to passively drain off any remaining blood while minimizing evaporative weight loss.



Figure 1: Incision

The fetal thymuses appeared soft, friable, lobulated and light pink in colour. The two lobes are connected and fused with each other.



Figure 2: Thymus in situ

In the present study, all the specimens were located in superior and upper part of anterior inferior mediastinum extending from root of neck to the level of 3<sup>rd</sup> costal cartilage. However in one specimen 20 weeks of gestation, a solid thymic cord was extending upward to cervical region behind sternohyoid and sternothyroid muscles. It was continuous with the mediastinal thymus with its right lobe. (Photograph-3)



Figure 3: Thymus

The thymic cervical prolongation was confirmed by histology. The specimen was dissected and processed in paraffin. sections were stained by Haematoxylin and eosin (H and E). Under microscope it showed normal thymic structure. Capsule is invaginated to form interlobular septa, dividing the thymus into various lobules. Lobules were divided into outer cortex, densely packed with lymphocytes and inner medulla, loosely packed with lymphocytes and containing Hassall's corpuscles. (Photograph-4) No other gross anomaly was observed in the fetus.

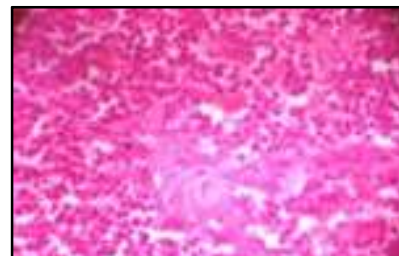


Figure 4: Microphotograph of thymus

## DISCUSSION

The first stage of thymic development is seen bilaterally in the third pharyngeal pouch towards the end of 6<sup>th</sup> gestational week, when endodermal cells form a sacculatation. The lower ends enlarge and unite superficially at 8<sup>th</sup> week. The lower ends are attached to the pericardium and gradually sink with it to a permanent position in thorax where it is located in the superior and anterior inferior mediastinum, the lower border reaches up to 4<sup>th</sup> costal cartilage.<sup>3,4</sup> Ectopic thymic tissue arises as a consequence of migrational defects during thymic embryogenesis. Thymus traverses the neck during the fifth to eighth week of embryological development prior to entering its definitive location into the superior

mediastinum. During this descent along the thymopharyngeal tract, there is a potential for thymic rests to be deposited in the neck.<sup>17</sup> This accessory thymus, like the normal thymus, undergoes hyperplasia during the first years of life and may present as a cervical mass of variable dimensions. In case of remnants of thymic tissue along the thymopharyngeal duct, the ectopic or accessory thymus is usually associated with a normally located thymus in the superior mediastinum. In rare cases, the thymus fails to descend or descends incompletely resulting in an entire thymus remaining in the cervical region.<sup>18-21</sup> Functionally, the thymus plays an important role in the development of the immune system. It has been established that the thymus is the central organ for T lymphopoiesis. So, in case of an isolated cervical ectopic thymus, surgery should be avoided as it results in an impairment of the immune system. An ectopic thymus can either be cystic or solid. A solid ectopic thymus only constitutes 10% of all ectopic thymus masses. Solid ectopic cervical thymus tends to be found primarily in infants whereas thymic cysts occur in a wider age range.<sup>19,20,22</sup> Most of these lesions are asymptomatic. Symptoms due to mass effect on trachea and/or esophagus such as stridor, dyspnea and/or dysphagia are rare.<sup>19,20,22,23</sup>

The disruption of thymic descent can result in an ectopic thymus (*ectopia thymi*) or cervical extension of thymus (*textus thymicus accessorius, lobuli thymici accessorii*) localized anywhere from the mandibular angle to the upper mediastinum. An ectopic thymus localized in the cervix is often called also "*thymus cervicalis*". The cervical thymus is a distinct entity from cervical extension of thymus. The basic difference is that in a case of ectopic thymus there is no thymus gland localized in its normal position. An ectopic thymus does not usually cause severe clinical symptoms. On the other hand, cervical remnants of thymic tissue have been found in up to 30% of infants studied at autopsy. Genetic research has confirmed theory that the migration of thymic primordia is controlled by neural crest-derived cells, which are present as an ectomesenchyme on the surface of these primordia. Patients with a deletion in the HOX family of transcription factors (expressed by neural crest cells) have a normal sized thymus, but in general, it is located above its normal position. Various types of cervical thymus may be present as a neck mass, usually laterally, from the angle of the mandible to the manubrium. Since it is rare to diagnose this entity before its surgical removal, the differential diagnosis includes the more common pharyngeal cleft cyst, thyroglossal duct cyst, cystic hygroma, cystic dermoid and lesions of the salivary gland as well as thyroid and parathyroid glands and cervical lymph nodes.<sup>24</sup> The cervical thymic lesions include the

following categories distinguished by anatomic location and the nature of the thymic gland tissue.<sup>25</sup> *Accessory Cervical Thymus*. Solid cervical thymic tissue is sequestered from the main gland, along the normal descent path, with or without parathyroid. Previous terms include aberrant, ectopic, undescended, persistent, or accessory thymus. *Cervical Thymic Cyst*. Sequestered cystic cervical thymus is found along a normal path of descent, with or without parathyroid glands. It is a cystic version of accessory cervical thymus and may have fibrous band or a solid thymic cord connection to the pharynx or mediastinum. *Undescended Cervical Thymus*. This occurs when a solid lobe of thymus fails to descend entirely, with or without a parathyroid complex. It differs from accessory cervical thymus in that only half of the normally blobbed thymus is present in the mediastinum; conceivably, it may also become cystic. *Persistent Thymopharyngeal Duct Cyst*. This is the same as undescended cervical thymus; however, the thymic duct is cystic. The thymus is solid, with or without parathyroid complex, and probably represents undescended thymus. A variant would be the cervical cystic duct leading to the mediastinal thymus. *Persistent Thymic Cord*. This is the cervical prolongation of a solid thymic cord which is continuous with the mediastinal thymus. The cystic variant may overlap with the histology and clinical appearance of the cervical thymic cyst if a true connection to mediastinal thymus cannot be documented. *Cervical Extension of Mediastinal Thymus*. This appears as low midline solid thymus at the thoracic inlet due to incomplete mediastinal descent. It may transiently present with increased intrathoracic pressure. *Ectopic Thymus*. This is the rare, solid thymic tissue in abnormal locations, for example, in the pharynx, trachea, or base of skull.<sup>26,27</sup> Hollinshead (1971) mentioned that the upper pole of one or both lobes of the thymus extend upwards in the neck to the level of thyroid gland or beyond it. Such an extension represents failure of the thymus to complete its migration into the thorax.<sup>28</sup> Stranding S *et al.* (2008) also reported that in some cases the upper pole of thymus reaches the inferior pole of the thyroid gland.<sup>3</sup> Ajita *et al.* (2006) found in one specimen of 24<sup>th</sup> week that the upper pole of thymus reaches to the lower pole of thyroid gland.<sup>29</sup> An isolated mass of thymic tissue may persist in the neck often close to an inferior parathyroid gland. This tissue breaks free from developing thymus as it migrates caudally in the neck. Variation in the shape of the thymus may exhibit slender cords or prolongation into the neck on each side anterolateral to trachea. These processes may be connected to the inferior parathyroid by fibrous strands.<sup>30</sup> In some new born infants the thymus may also extend superiorly through the superior thoracic aperture into the neck and compress the trachea.<sup>31</sup> *Seid Abbas*

*Tabatabaie et al* evaluated 90 patients without any thymic disease and found ectopic thymic tissue in the neck of 4.455% of them.<sup>5</sup> Ashour reported forty patients with myasthenia gravis who underwent maximal thymectomy. Complete histological study findings were available for 38 patients. The prevalence of ectopic thymic tissue was 39.5% (15 of 38), 63.2% of which was in the neck and often near the thyroid gland.<sup>32</sup> Jaretzki and Wolff studied 50 cases of myasthenia gravis and the incidence of ectopic foci of thymic tissue in the adipose tissue of the neck was 32.0% and in the mediastinum 98.0%.<sup>33</sup> Masaoka and colleagues found 72.2% ectopic thymic tissue in the mediastinum of 18 myasthenia gravis patients.<sup>34</sup> Thymic tissue was found in the anterior mediastinal fat in 12 subjects (44.4%), in the retrocarinal fat in two (7.4%), and in the preaortic fat in none.<sup>35</sup> Yamashita reported cervical ectopic thymic tissue macroscopically in 12 out of 657 patients with Basedow's disease (1.8%).<sup>36</sup> In the study of Zieliński *et al*, overall, ectopic foci of thymic, or probably thymic tissue were found in 56.9% of patients. The ectopic foci were most prevalent in the aortopulmonary window (25.9%), the right pericardiophrenic fat pad (24.1%), the perithymic tissue (22.4%), and the left pericardiophrenic fat pad (22.4%). The ectopic foci were slightly less prevalent in the aorta-caval groove (17.2%) and in the neck (with Hassall's corpuscles 0 and without Hassall's corpuscles 12.1%).<sup>37</sup> Pages studied 763 autopsies of fetuses of various ages, newborns, infants, and surgical samples of 8 children and adults and found 72 (9.4%) cases of cervical ectopic thymic tissue.<sup>38</sup> Adriana HANDRA-LUCA reported a case of 64-year-old man presented with elevated thyrocalcitonin, and a history of resected thyroid medullary carcinoma. Cervical thymus was detected incidentally in the neck dissection resection specimen for thyroid medullary carcinoma extension. This case was peculiar due to the presence of a thymic microcyst and the coexistence of parathyroid tissue along with the thymic lobules. Persistent hypocalcaemia, requiring calcium intake, occurred after resection. Although rare, the presence of such neck branchial arch abnormalities should be considered for a successful management of extensive malignant thyroid tumours.<sup>39</sup> Cervical extension of the thymus is often mistaken for a soft tissue mass in the neck, particularly in children and young adults. The problem in differentiating thymic tissue from a mass is compounded when the thymus is hyperplastic and shows increased fluorodeoxyglucose uptake. We describe the case of a child on follow-up for Ewing sarcoma in whom we detected an avid thymic extension in the neck, which mimicked recurrent disease both anatomically and functionally.<sup>40</sup> Clinically, in most cases, ectopic thymic tissue presents as a unilateral, asymptomatic neck mass,

commonly in the left side of the neck.<sup>4,7</sup> However, there are some reports connecting ectopic thymic tissue to respiratory distress<sup>8,9</sup> and tracheal obstruction,<sup>9</sup> to dysphagia,<sup>3</sup> to infection and sudden enlargement due to upper respiratory tract infection,<sup>9,10</sup> to laryngeal displacement, to myasthenia gravis<sup>11</sup> and to malignancy.<sup>12,13</sup> Ectopic thymic cyst in the neck.<sup>41</sup>

## CONCLUSION

High division of sciatic nerve is very important anatomical variation which should be kept in mind by surgeons as well as physician. there are reports which associate ectopic thymic tissue to respiratory distress, tracheal obstruction, dysphagia, infection and sudden enlargement due to upper respiratory tract infection, laryngeal displacement, myasthenia gravis<sup>11</sup> and malignancy.

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